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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KELLY, ROBERT M	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,732	ZINN ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-124 and 126-165* is/are pending in the application.

4a) Of the above claim(s) *1-123,126-129,133 and 135-151* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *124,130-132,134 and 152-165* is/are rejected.

7)☒ Claim(s) *124,164 and 165* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to restriction requirement and amendment of 7/17/09 are entered.

Claims 124, 126, and 127 are amended.

Claim 125 is cancelled.

Claims 1-124 and 126-165 are presently pending.

Election/Restrictions

Applicant's election with traverse of Group VII, and the species of SEQ ID NO: 9 in the reply filed on 7/17/09 is acknowledged. The traversal is on the ground(s) that (i) the search and examination does not constitute a serious burden, as is required under MPEP section 803; (ii) there is a unity of invention; (iii) there is no serious burden on the Examiner for the species listed. This is not found persuasive because, respectively, (i) there is a serious burden, as the special technical feature is broken, and each invention requires distinct considerations; (ii) there is no unity of invention as shown in the restriction requirement; and (iii) the species constitute a serious burden as the structure of each is distinct and as shown in the special technical feature analysis of the restriction requirement, there is one species which meets the special technical feature. Lastly, it should be noted that this is a restriction under 1.142, not 111, and hence, does not require "serious burden" analysis, but a lack of unity analysis.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-123, 126-129, 133, 135-151 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and species, there being no

allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/17/09.

Claims 124, 130-132, 134, and 152-165 are presently considered, only with respect to the elected invention (nucleic acid administration, and SEQ ID NO: 9).

ABSTRACT

Although not objected-to, the abstract is presented as the first page of the PCT priority publication. Prior to publication, a copy of the abstract is required to be sent by amendment, for publication purposes. Hence, it is suggested that Applicant simply supply a clean page amendment with the same abstract.

Claim Objections

Claims 124, and 165 are objected-to for encompassing non-elected inventions. To wit, the claims encompass, e.g., Group VI inventions, as shown in the restriction requirement of 2/18/09.

Claim 164 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 164 limits the vector to AAV, while Claim 163, from which it depends limits the vector to an adenoviral vector. These are distinct vectors, albeit they have a common limitation in their names: "adeno". Adenoviruses are episomal viruses, while adeno-associated viruses, are distinct for being integrating as well as having a distinct envelope, and

were simply named for their association of being found active when an adenovirus infection occurs in the same cell.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 165 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 165 is rejected for depending from a cancelled claim, and hence, its metes and bounds are indeterminate. However, for purposes of compact prosecution, the claim will be considered to depend from Claim 124.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 130-134, 152-165 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for operably-linked expression control sequences comprising a promoter to the encoded protein sequence, does not reasonably provide enablement for an absence of an operably-linked promoter or the simple operable linkage of any expression control element. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's claims encompass reducing inflammation in a subject, by the administration of a nucleic acid encoding a complement modulator, which inhibits complement activation. Dependent Claim 161 indicates that all the broader claims do not require an operably-linked promoter.

In addition, the breadth of expression control sequence, in its broadest reasonable interpretation, encompasses more than promoters. It should be noted that Applicant was able to adequately express the term promoter (e.g., paragraph 19 of the specification Publication). Hence, it would appear that Applicant intentionally wishes even Claim 161 to simply include any expression control element, e.g., only an enhancer, or a translation initiation sequence, or a polyA tail, or anything which, in some context, helps to control expression.

However, as is very well known in biological applications, a promoter is required to be operably-linked to a coding sequence in order to obtain translation and a translation initiation sequence to initiate translation.

Further, the confluence of Applicant's specification fails to teach nucleic acids which inhibit complement activation, or even modulate inflammation. The Art fails to teach the same.

Hence, the Artisan would have to experiment to determine which coding sequences themselves act to inhibit inflammation, and do so through inhibiting complement activation. Further experimentation would be required to determine those non-promoter-linked coding sequences which will allow for transcription and translation to occur.

Such experimentation is undue as it amounts to inventing the breadth of Applicant's claimed subject-matter.

Hence, the claims are rejected for lacking a fully enabled scope.

I. Base Rejection: retroviral vectors with a generic complement inhibitor on its surface. This demonstrates the non-allowability of the broad claim as compared to the various species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 124, 152, 160, and 161 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,643,770 to Mason, et al.

Mason teaches transforming tissues *in vivo* (e.g., Summary of the Invention), with retroviral vectors with gp70 envelope glycoproteins (e.g., Id., paragraph 3) which are chimerically expressing complement inhibitors (Id.), e.g., those found in pathogens (CIMs) (e.g., BACKGROUND, V. Inhibitors of the Complement System). In addition the vector which is administered is a retroviral vector (Summary of the Invention), and can have the gene encoding the gp41-CIM in the genome and linked to the expression control sequence (e.g., Id., paragraph 1). Still further, if enablement is to be questioned, it appears that the claims encompass the same complement inhibitors (e.g., Claims 1 and 8, and definition of "complement inhibitor" in

specification, paragraph preceding Section IV., The Complement System), and still further, Claim 13, compared to Claim 14, demonstrates that Claim 13 specifically encompasses *in vivo* administrations.

II. Modifications of the Retroviral Base Rejection to Utilize Adenoviral Vectors

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 152, 160, 161, and 163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al.

As shown above, Mason teaches expression of fusion proteins to place a complement inhibitor onto the surface of a retroviral vector and use to transform tissues. However, Mason does not teach the use of adenoviral vectors.

On the other hand, it is well known that adenoviral vectors suffer from complement-mediated inactivation (e.g., Xing, et al. (2001) Cell Research, 11(2): 116-24, figure 5B). Moreover, it is well known to link peptides to be displaced on the surface of an adenovirus (e.g., U.S. Patent No. 7,468,181 to Vogels, et al., paragraph 6 of the Detailed Description, describing the addition of peptides to several surface displayed proteins of adenoviruses).

Hence, it would be obvious to modify the Mason to utilize adenoviral vectors. The Artisan would do so to provide adenoviral vectors for administration and avoid complement-mediated inactivation. Moreover, the Artisan would have had a reasonable expectation of success, as it was already to so-display peptides, and Adenoviruses are well known for gene delivery.

III. Modification of (II) to Utilize a Hypervariable Region

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 152, and 160-163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to claims 124, 152, 160, 161, and 163 above, and further in view of U.S. Patent No. 6,127,525 to Crystal, et al.

As shown above, the various references make obvious the claims, except the aspect of utilizing a hypervariable region for inserting the peptide.

Crystal demonstrates that several hypervariable regions of adenovirus may be deleted and/or substituted with chimeric peptides (e.g., paragraphs 11-12 of the section titled "Chimeric Adenovirus Coat Proteins").

As such the Artisan would find the invention obvious over the art. The Artisan would modify the references as Crystal demonstrates that these regions are tolerant to changes and it would place the peptide on the surface of the virus. Moreover, the Artisan would have a reasonable expectation of success, as Crystal teaches it would work, and Mason teaches that the peptides would work to ameliorate the complement inactivation of the virus.

IV. Modification of (II) or (III) to utilize ED1

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 152, 160, 161, and 163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al as applied to claims 124, 152, 160, 161, and 163 above (II), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34; and

Claims 124, 152, and 160-163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., and U.S. Patent No. 6,127,525 to Crystal, et al., as applied to claims 124, 152, 160-163 above (III), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34.

As shown above, the various references make obvious the invention in each case, except that the references do not teach or make obvious the ED1 domain.

On the other hand, Inal teaches that the ED1 domain of Sh-TOR inhibits complement and does so when isolated from the normal protein (e.g., ABSTRACT).

Hence, it would be obvious to modify the references to arrive at the invention. The Artisan would do so to inhibit complement inactivation of the virus. Moreover, the Artisan would have a reasonable expectation of success, as Inal has shown that the peptide works out of context.

V. Modification of (IV) to Further Include a His-Tag

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 152, 154, 160, 161, and 163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 152, 160, 161, and 163 above (II), and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74; and

Claims 124, 152, 154, and 160-163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research,

11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 152, 160-163, and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74.

As shown above, the various limitations are obviated, except that of utilizing a His-Tag.

However, it was well known in the Art that His-Tagged entities can be isolated utilizing the His-Tag (e.g., Huang, ABSTRACT).

Hence, it would have been obvious to modify the invention to include a His-Tag. The Artisan would do so to provide for easier isolation of the viruses with such ED1 expressed on its surface. Moreover, the Artisan would have a reasonable expectation of success, as it was well known to use His-Tags to isolate entities with such His-Tag.

VI. Modification of V to Utilize 2 ED1 Sequences and a Linker

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that the following rejections rely upon Oh, et al., which is a reference under 102(a), and hence, may be sworn behind to overcome the rejection.

Claims 124, 152-154, 160, 161, and 163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., Inal, et al. (2000) FEBS Letters, 470:

131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124, 152, 153, 154, 160, 161, and 163 above, and further in view of Oh, et al., (2003) Immunology, 110: 73-79; and

Claims 124, 152-154, and 160-163 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124, 152-154, and 160-163, and further in view of Oh, et al., (2003) Immunology, 110: 73-79.

As shown above, the various limitations are obviated, except the use of 2 ED1 sequences, linked by a linker.

On the other hand, Oh teaches that a duplicated ED1 domain provides increased inhibition of complement activation over that of a single ED1 domain (p. 76, col. 2, paragraph 2). In addition, the linker may be as little as a peptide bond, given the broadest reasonable interpretation, and also, Oh teaches that amino acid 27 is not important, but is necessarily present in their homodimer (p. 78, paragraph 1).

Hence, it would have been obvious to modify the references to utilize Oh's ED1 duplicated domain. The Artisan would do so to increase complement inhibition. Moreover, the Aritsan would expect success, as Oh teaches that complement inactivation is greater than single ED1 domains.

VI. Modification of (II) to Utilize an AAV vector (AAV vector in AdV envelope)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It should be noted that Applicant may argue that the following rejection demonstrates proper dependency for Claim 164, as the AAV vector is within an Adenovirus envelope, however, the vector is the vector, and the envelope is the envelope in this case, and hence, it is still considered an improper dependency. The base claims to adenovirus are still included as the added reference does not negate the obviousness of the base rejection, made in (II).

Claims 124, 152, 160, 161, 163, and 164 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 152, 160, 161, and 163, further in view of Goncalves, et al. (2001) Virology, 288(2): 236-46.

As shown above, the references obviate the claims, except the use of an AAV vector.

Goncalves, however, teaches encapsulation of AAV vectors into Adenoviral envelopes, to thereby allow superior prolonged transgene expression and allowing larger inserts (e.g., ABSTRACT). Moreover, the transgenes for packaging from adenovirus are entered into the AAV genome (e.g., ABSTRACT).

Hence, it would have been obvious to make the invention as claimed. The Artisan would do so to increase the the time of transgene expression and allow larger inserts than AAV enveloped AAV vectors. Moreover, the Artisan would expect success, as Goncalves teaches it can be done.

Claims 130-134 and 155-159 are Free of the Prior Art

It should be noted that SEQ ID NO: 8 and SEQ ID NO: 9 were searched in the prior Art, and it was found that nothing anticipates the claimed sequences. Further, it should be noted that Oh, et al., (2003) Immunology, 110: 73-79, and reference with a 102(a) date, while suggesting several mutations to the ED1 region (Figure 4), does not teach or suggest the combinations of mutations encompassed, but does help to enable the variations in sequence identity claimed.

Suggestions for Allowability

The Examiner suggests that Applicant amend the claims to include the specific sequences expressed on the surface of the virus for an allowable claims to any virus, as well as requiring a promoter to be linked to the encoded sequence.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633